DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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June 9, 2015

Siemens Healthcare Diagnostics Inc.
c/o Ms. Asha Gartland
Technical Regulatory Affairs Specialist
511 Benedict Avenue
Tarrytown, NY 10591

Re: k143639
Trade/Device Name: IMMULITE® 2000 CEA Calibration Verification Material
Regulation Number: 21 CFR 862.1660
Regulation Name: Quality control material (Assayed and Unassayed)
Regulatory Class: Class I, Reserved
Product Code: JJX
Dated: December 19, 2014
Received: December 22, 2014

Dear Ms. Gartland,

This letter corrects our substantially equivalent letter of January 23, 2015.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21

CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Leonthena R. Carrington -S

Leonthena Carrington, MS, MBA, MT(ASCP)
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K143639

Device Name
IMMULITE® 2000 CEA Calibration Verification Material

Indications for Use *(Describe)*
The IMMULITE® CEA Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE CEA assay on the IMMULITE 2000 systems.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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SIEMENS

Section 006: 510(k) Summary

510(k) Summary

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: K143639

1. Submitter	
Mailing Address:	Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591
Contact Person:	Asha Gartland Technical Regulatory Affairs Specialist
Phone Number:	(914)-524-3257
Fax Number:	(914)-524-2101
E-mail Address:	asha.gartland@siemens.com
Date Prepared:	January 20th, 2015
2. Device Name	
Proprietary Name:	**IMMULITE® 2000 CEA Calibration Verification Material**
Measurand:	Quality Control materials for IMMULITE® 2000 CEA assay Calibration Verification Material (CVM) for IMMULITE® 2000 CEA
Type of Test:	assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Immunology (82)
3. Predicate Device Name	IMMULITE® 2000 DHEA-SO4 Calibration Verification Material (CVM)
Predicate 510(k) No:	K140258
4. Device Description:	The CEA Calibration Verification Material (CVM) contains one set of four vials each 1.0mL after reconstitution. CVM1 contains lyophilized processed human serum with preservatives. CVM2, CVM3 and CVM4 contain various levels of human CEA in a lyophilized processed human serum matrix with preservatives.

5. Intended Use:	See Indications for Use Statement below:
Indication for Use:	The IMMULITE® CEA Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE CEA assay on the IMMULITE 2000 systems.
Special Conditions for Use Statement(s):	For prescription use only
Special Instrument Requirements:	IMMULITE® 2000 Systems
6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:	A comparison of the device features, intended use, and other information demonstrates that the IMMULITE® 2000 CEA Calibration Verification Material (CVM) is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: Substantial Equivalence Comparison

SIMILARITIES		
	Candidate Device IMMULITE 2000 CEA CVM	**Predicate Device IMMULITE 2000 DHEA-SO4 CVM**
Intended Use	The IMMULITE® CEA Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE CEA assay on the IMMULITE 2000 systems.	The IMMULITE® DHEA-SO4 Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE DHEA-SO4 assay on the IMMULITE 2000 systems.
Form	Lyophilized	Same
Storage	≤-20°C	Same
Matrix	Human Serum with preservatives	Same
Stability	Stable unopened until the expiration date	Same
Levels	4	Same
Use	Single Use Only	Same

	DIFFERENCES	
	Candidate Device IMMULITE 2000 CEA CVM	**Predicate Device IMMULITE 2000 DHEA-SO4 CVM**
Analyte	CEA	DHEA-SO4

7. Non-Clinical Performance Testing

Performance testing has been carried out to demonstrate that this device meets the performance specifications for its intended use. The following tests were performed on the candidate device.

7.1 Stability Summary:

The stability study was conducted to validate real-time shelf life and open component (in-use or open vial) claim for the IMMULITE 2000 CEA Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM before and after reconstitution.
The IMMULITE® 2000 CEA Calibration Verification Materials are stable up to 6 years when stored at -20°C prior to opening and for 8 hours at ambient or room temperature (15-25°C) after reconstitution.

7.1.1 Stability Protocol Summary:

The CVM study protocols are run as part of the calibrator stability testing. Three lots of stability CVMs and reference CVMs are run in duplicate (as a minimum) at the time points shown in **Tables 2a, 2b and 2c** and the dose value determined from the reference calibrator curve.

Table 2a: Stability Time Points for CEA CVM lot 006

CVM level	Time-Points (months)			
LCECVM1	Day 0	60	72	108
LCECVM2	Day 0	60	72	108
LCECVM3	Day 0	60	72	108
LCECVM4	Day 0	60	72	108

Table 2b: Stability Time Points for CEA CVM lot 007

CVM level	Time-Points (months)			
LCECVM1	Day 0	48	60	84
LCECVM2	Day 0	48	60	84
LCECVM3	Day 0	48	60	84
LCECVM4	Day 0	48	60	84

Table 2c: Stability Time Points for CEA CVM lot 090

CVM level	Time-Points (months)			
LCECVM1	Day 0	4	5	6
LCECVM2	Day 0	4	5	6
LCECVM3	Day 0	4	5	6
LCECVM4	Day 0	4	5	6

For Open Component testing, the results are determined from a 2-point adjustment. Using IMMULITE 2000 CEA kit lot 290, CEA CVM lot 090 was tested at 2-hourly intervals for up to 9 hours at ambient or room temperature (15-25°C) conditions and compared to the determinations at time zero.

7.1.2 Stability Acceptance Criteria Summary:

The guideline criteria for samples stored over time at -20°C is outlined in **Table 3**.

The Acceptance Criteria for the IMMULITE CEA CVM real time and open component stability testing is applied to dose compared to dose at time point zero. The result is required to fall between ±10% difference for CVM levels 2 and 3 and ±15% for CVM level 4.

If the guideline criteria fail, then the stability is assessed on analyte drift as described below:

- If the slope is not significant ($p \geq 0.05$), the stability estimate is the study duration less one time unit.
- If the slope is significant ($p < 0.05$), the stability claim estimate is taken as the time at which the one-sided 95% confidence interval of the regression line intersects with the allowable drift limit for the specific sample.
- The minimum stability estimate across all samples is taken as the stability estimate for that lot.
- The final stability claim for the product is taken as the minimum estimate across all lots from the trend analysis results.

The acceptance criterion is summarized in **Table 3**.

Table 3 Acceptance criteria for stability of IMMULITE 2000 CEA CVM

CVM level		Dose at time point 0 (ng/mL)	Guideline Criteria % difference to dose at time point 0	Acceptable dose range (ng/mL)
LCECVM1	006	0.00	Not Applicable	≤0.2
	007			
	090			
LCECVM2	006	3.04	±10%	2.74 – 3.34
	007	2.54		2.28 – 2.79
	090	3.04		2.74 – 3.34
LCECVM3	006	94.2	±10%	84.8 – 103.6
	007	91.7		82.5 – 101
	090	96.7		87.0 – 106
LCECVM4	006	633	±15%	538 - 728
	007	602		512 - 692
	090	596		507 - 685

7.2 Traceability:

The IMMULITE CEA CVMs are traceable to an internal standard. The CVMs are manufactured using qualified materials and measurement procedures.

7.3 Value Assignment:

IMMULITE CEA CVMs are 4 level materials which are a subset of 7 level CEA calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of CEA reagents and two point adjustors.

The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The assigned reference calibrators are prepared using CEA antigen stock and are traceable to an internal standard which have been gravimetrically prepared. Nine levels of commercially available controls and 21 samples (5 normal and 21 spiked samples) were used to validate calibrator/CVM value assignments.

The CVMs are manufactured using qualified materials and measurement procedures. The IMMULITE CEA calibrators/CVMs were tested on 27 replicates in total, comprised of 9 runs, 3 replicates per run, 9 IMMULITE 2000 systems and 5 different reagent kit lots.The CVMs dose values are generated using curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered values for each run on each instrument independently. CVM values are then averaged across all systems. Quality control is performed by calculating the recovery of patient samples and controls using the assigned CVM values. The controls must fall within their target ranges.

7.4 Expected Values/Reference Range:

Each CVM level was tested on tested on 27 replicates in total, comprised of 9 runs, 3 replicates per run, 9 IMMULITE 2000 systems and 5 different reagent kit lots. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2 Standard Deviation (SD). The expected values are provided in the IMMULITE® 2000 CVM Calibration Verification Material lot-specific package insert.

The expected assay range is up to 550 ng/mL. The target values in **Table 4** can be considered as guidelines.

Table 4: Target Values

Analyte target levels	**CVM Level**	**Target Mean (ng/mL)**	**Standard Deviation (SD)**	**Guideline ±2SD Range (ng/mL)**	
	LCECVM1	0.00	-	0.00	≤0.20
	LCECVM2	2.51	0.25	2.01	3.01
	LCECVM3	92.0	5.5	81	103
	LCECVM4	600	45	510	690
Assay Range	Up to 550 ng/mL				

Each laboratory should establish their limits for acceptability based on methodology, clinical significance and medical decision levels of the test analyte. The representative, total precision tabulated in the respective assay instructions for use may be considered as one factor when establishing local, acceptable ranges. The values provided above may be considered as guidelines. Value assignment is lot specific.

Standard/Guidance Documents Referenced**:**

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

Proposed Labeling**:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

8. Conclusion:

The IMMULITE® 2000 CEA Calibration Verification Material is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the FDA cleared IMMULITE® 2000 DHEA-SO4 Calibration Verification Material. The substantial equivalence of the device is supported by the non-clinical testing and was found to be comparable and supports the claims of substantial equivalence, product safety and effectiveness. Based on the testing completed and the comparisons with predicate device, the IMMULITE® 2000 CEA Calibration Verification Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.